Remarks/Arguments

A. Summary of the Claims

Claims 1-5 and 12 are amended, and no claims have been cancelled or added. Support for the amendments can be found throughout the specification and claims as originally filed. For instance, claim 1 is amended to specify that the compacting step (b) is performed in a roller compactor apparatus. This is supported in the specification as filed, more specifically in the claims as filed.

Claims 1 to 5 are amended to specify that the multiple powdered active ingredients to be part of the pharmaceutical dosage forms have distinct mean particle sizes. Non-limiting support for this amendment can be found on page 1 in paragraphs [0003] and [0004], wherein Diclectin® is cited as an example of a medicament with two active ingredients in the form of powders having different granular sizes.

A typographical error in each one of claims 1, 2, and 12 is corrected.

Claims 1-12 are pending in this case.

B. The Obviousness Rejection Is Overcome

1. Summary of the Rejection and Summary of Applicant's Arguments

Claims 1-12 are rejected under 35 U.S.C. 103 § (a) as being obvious over Chen (US Pat. 5,260,069) in view of Chu *et al.* (US Pat. 6,419,954) and Bishai *et al.* In summary, the Examiner contends that the primary reference, Chen, "...discloses unit dosage forms for delivering drugs into the body in a series of sequential, pulsatile releasing events. Such unit dosage forms may be prepared using a roller compacting method." Action at page 2. As for Chu *et al.*, it is relied upon for apparently disclosing "....embodiments in which a tablet can further include untreated active agents (e.g., without coating material or powders) in addition to the active agent-

containing particles and that the active agent particles can contain vitamins or drugs...." *Id.* Bishai *et al.* is cited as disclosing "...the combination of 10 mg doxylamine succinate and 10 mg pyridoxine HCl is safe and effective in treating nausea and vomiting associated with pregnancy." *Id.* at page 3.

The Examiner concedes that the cited art fails to "disclose the use of more than one active ingredient, such as the combination of doxylamine succinate and pyridoxine HCl." *Id.* In an effort to supplement the deficiencies of the prior art, it is contended that a person of ordinary skill in the art "...would have been motivated to modify the prior art as above with the expectation that the combination of doxylamine succinate and pyridoxine in granules prepared by roller compaction and sieving to obtain appropriate mesh size would be safe and effective in treating NVP." *Id.*

Applicant disagrees. The claims, prior to any amendment made above, were not rendered obvious by the cited references. However, in an effort to further the prosecution and secure prompt allowance, claim 1 has been amended to specify that the compacting step (b) is done in a roller compactor apparatus, and independent claims 1-5 have been amended to specify that the multiple powdered active ingredients have distinct mean particle sizes. As explained in the following section, the cited art references fail to disclose at least this aspect of the present invention. This alone overcomes the obviousness rejection. MPEP § 2143.03 ("To establish a prima facie case of obviousness... the prior art reference (or references when combined) must teach or suggest all the claim limitations.") Further, there is no motivation to modify or combine the references, and there is no reasonable expectation of success that such modifications or combinations would work. *Id.*

2. The Prior Art Fails to Disclose "multiple powdered active ingredients comprising distinct mean particle sizes"

Applicant submits that both Chen and Chu *et al.* focus on the technical problems of obtaining either a "pulsatile" (Chen at Abstract) or a "modified" (Chu *et al.* at Title and Abstract) release of the active ingredient, and thus on the composition of the membrane, coating or gel-forming matrix that surround the pellets or particles before compression. Such technical problems are different from that of the present invention, namely to alleviate ingredient loss during the manufacturing of heterogeneous powderous multi-ingredient medicaments and to provide superior content uniformity results (Applicant's specification at page 2, ¶[0006]). Further, these references do not appear to disclose "pharmaceutical dosage forms comprising multiple powdered active ingredients comprising distinct mean particle sizes"—much less a method for preparing such dosage forms.

As for Bishai *et al.*, it appears to disclose that the combination of both doxylamine succinate and pyridoxine hydrochloride (as found in Diclectin™) is safe and effective in the treatment of nausea and vomiting during pregnancy. Bishai *et al.* at pages 167, 170, 173-177. Bishai *et al.* fails to disclose or suggest any aspect of a method for preparing a formulation including these active ingredients—much less Applicant's claimed method of preparing "pharmaceutical dosage forms comprising multiple powdered active ingredients comprising distinct mean particle sizes."

Thus, all of the cited references fail to disclose or even suggests the technical problem of having "multiple powdered active ingredients comprising distinct mean particle sizes" involved in a process of preparation of a pharmaceutical dosage form. Therefore, the present obviousness rejection is overcome and should be withdrawn. MPEP § 2143.03.

3. There Is No Motivation to Modify the Cited References To Obtain Applicant's Claimed Invention

A person of ordinary skill in the art would not find, in any of the cited references, or in the knowledge generally available to him or her, any suggestion or motivation to modify Chen or to combine its teachings with Chu *et al.* and Bishai *et al.* to obtain Applicant's claimed invention.

For instance, Chu *et al.* explains that "any suitable granulation methods can be used to produce particles comprising an active agent." Chu *et al.* at col. 12, lines 25-26. Either wet or dry granulation methods can be used. *Id.* at col. 12, lines 29-31. These statements confirm that several possible techniques are contemplated. Stated another way, there is no motivation to use Applicant's claimed "method for the preparation of pharmaceutical dosage forms comprising multiple powdered active ingredients comprising distinct mean particle sizes." See MPEP § 2143.01 ("The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination.") (underlines in original). Further, Applicant respectfully notes that "obvious to try" is not the appropriate standard under 35 U.S.C. § 103. *The Gillette Co. v. S.C. Johnson & Son, Inc.*, 919 F.2d 720 (Fed. Cir. 1990) (noting that "'obvious to try' is not to be equated with obviousness under 35 U.S.C. 103.").

In addition, as acknowledged by the Examiner, Chen and Chu *et al.* both fail to disclose or suggest the use of more than one active ingredient in the preparation of granules, particles, or pharmaceutical dosage forms. Further, as explained above, there is no disclosure in the cited references to use "multiple powdered active ingredients comprising distinct mean particle sizes" in the preparation of a pharmaceutical dosage form. This is evidence that there is no reasonable

expectation of success that modifying or combing the cited references to obtain Applicant's claimed invention would work.

In view of the above, it is clear that a person of skill in the art would not have been motivated to modify Chen or to combine its teachings with Chu *et al.* and Bishai *et al.* to obtain Applicant's claimed invention. Further, there is no reasonable expectation of success that such a combination or modification would work. Therefore, at least two additional elements necessary to establish a *prima facie* case of obviousness are missing.

Because all three elements necessary to establish a *prima facie* case of obviousness are missing, the present obviousness rejection is overcome. Therefore, Applicant requests that this rejection be withdrawn.

4. Additional Considerations

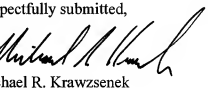
Applicant also notes that the roller compacting method provided surprising and unexpected results as to alleviation of ingredient losses during manufacturing of heterogeneous powdered active ingredients and as to content uniformity in terms of active ingredients (*see, e.g.*, Applicant's specification at page 5, ¶ [0014]). This is further evidence of non-obviousness. *See In re Pravin*, 54 F.3d 746, 750 (Fed. Cir. 1995) ("One way for a patent applicant to rebut a prima facie case of obviousness is to make a showing of 'unexpected results,' i.e., to show that the claimed invention exhibits some superior property or advantage that a person of ordinary skill in the relevant art would have found surprising or unexpected.").

C. Conclusion

Applicant believes that the present document is a full and complete response to the Office Action mailed June 30, 2006. The present claims are in a condition for allowance, and such favorable action is requested.

It is believed that no fee is due for filing this Response. However, should any fees under 37 C.F.R. §§ 1.16 to 1.21 be required for any reason relating to this document, consider this paragraph such a request and authorization to withdraw the appropriate fee from Fulbright & Jaworski Deposit Account No. 50-1212/GOUD:037US.

Respectfully submitted,



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